UNITED STATES PATENT AND TRADEMARK OFFICE

HL

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,663	04/11/2001	Anthony J. Polak	LFS-5044	1850

27777 7590 09/10/2004

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
YANG, NELSON C	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/832,663	POLAK ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/01, 03/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

I. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The limitation recited in claim 18 could not be found the disclosure.

1. The use of the trademarks ALKALI BLUE, SAFRANIN, PARAROSANILINE, ALEXA FLUOR, ALEXA-488, ALEXA-633, CY-5 have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

II. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 27, 28, 33, and 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that specify how deeply

the device may be implanted, what kind of biological fluid that the device would be in biological contact with, the wavelengths of light to irradiate the device, how the device would be irradiated when beneath the skin, the correlation between light emitted from the device and irradiation of the device, the correlation between the light detected and the presence of analytes.

In particular, it is unclear how deep the device could be implanted before it would be impossible to detect a signal from the device. It is also unclear if the device would function similarly or even function when in contact with different types of biological fluid such as blood, urea, saliva, etc. It is also unclear if infrared radiation such as body heat would interfere with method of detecting analytes with the device.

The light used to irradiate the device could potentially be absorbed by the body before it even reached the device, and even if it did reach the device, it is unclear if it would excite the labels in the device, particularly if a quenching dye was located in the membrane, absorbing the light. Furthermore, it is unclear whether the irradiation with a laser would necessarily excite the labels, or if applicant is limiting the labels to ones that would be excited with infrared light.

Even if a light was produced, it is unclear if the light would be related to analytes, as the reference would presumably produce a signal in addition to interference from infrared radiation such as body heat, and therefore it would be unclear how the light would be analyzed to distinguish between light emitted in the presence of an analyte, and light emitted in the absence of an analyte. It is also unclear if the light emitted would be capable of being detected, as it could also potentially be absorbed by the body before it could be detected.

Claims 21, 22, contain the trademark/trade names Alkali Blue, Safranin, and Pararosaliline. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe quenching dyes and, accordingly, the identifications/descriptions is indefinite.

4. Claims 27, 28, and 33 contain the trademark/trade names ALEXA-488, ALEXA-633, and Cy-5. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe label and reference dyes and, accordingly, the identification/descriptions are indefinite.

Claim Rejections - 35 USC § 103

III. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-17, 19-20, 23-26, 29, 34-47 are rejected under 35 U.S.C. 103(a) as being anticipated by Schultz [US 6,256,522] in view of Krauth [US 4,954,435].

With respect to claim 1-4, 7-8, 19, 20, 23-26, 29, Schultz teaches a receptor material, Concanavalin A covalently attached to Rhodamine dye molecules, analog analyte comprising dextran covalently attached to fluorescein dye molecules located within a transparent capsule comprising a semi-permeable membrane comprising cellulose or polysulfone (column 10, lines 21-37, claim 1). Schultz further teaches a pH indicator located within the capsule (column 11, lines 1-5, claim 1). The rhodamine quenches emission fluorescence from the fluorescein (column 10, lines 38-45). With respect to claim 4, the receptor material may be immobilized to a gel such as polyethylene glycol within the chamber (column 8, lines 11-27). Schultz fails to specifically teach that the pH indicator can be used as a reference.

Krauth, however, teaches that in fluorescence assays, using a ratio of light signals, one signal being the reporter signal, and the other being the reference signal, provides a correction mechanism for obviating such variables such as fluctuation in the lamp output, variation in tube position, diameter, or optical quality (column 3, lines 50-61).

Therefore it would have been obvious to add a reference as suggested by Krauth in the device of Schultz et al, in order to obviate such variables such as fluctuation in the

lamp output, variation in tube position, diameter, or optical quality when detecting the presence of analytes.

6. With respect to claims 5-6, although neither Schultz nor Krauth teaches a reference covalently bonded to the membrane or in the membrane, it would have been obvious to one having ordinary skill at the time was made to have the reference covalently bonded to the membrane or in the membrane, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse,* USPQ 70.

7. With respect to claims 9-12, Schultz teaches that the analyte and receptor may bind to form an analyte-receptor complex (column 6, lines 40-50) and comprise dextran (column 10, lines 20-37).

8. With respect to claims 13-17, Schultz teaches that the receptor material can be immobilized to a gel such as polyacrylamide (column 8, lines 20-28). Schultz further teaches that rhodamine dye molecules can be attached to the receptor material for quenching fluorescence (column 10, lines 25-45).

9. With respect to claims 34-36, Schultz teaches that the semi-permeable membrane comprising cellulose or polysulfone (column 10, lines 21-37, claim 1)

10. With respect to claim 37, Schultz teaches that the analyte-permeable membrane may also have a reflector comprising metallic particles immobilized on the surface of an ultrafiltration membrane (column 10, lines 1-10).

11. With respect to claims 38-39, Schultz teaches that the analyte being measured is glucose (column 10, line 25).

12. With respect to claims 40-43, while Schultz do not teach what the ratio of the empty space encapsulated by the capsule to a volume occupied by the binding substrate is, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Furthermore, since applicant has not discussed any unexpected improvements or results using ratios between 0.05 and 5, between 0.5 and 3, or 1, it would have been obvious to a person of ordinary skill in the art to have used ratios between 0.05 and 5, between 0.5 and 3, or 1 through normal optimization techniques.

13. With respect to claims 44-47, the sensor unit may be placed underneath the skin (column 7, lines 27-36), illuminated with a laser (column 7, lines 38-45), and measuring absorption of light, including ultraviolet, visible or infrared (column 7, lines 15-25).

14. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435], as applied to claim 1 above, and further in view of Vo-Dinh [US 5,864,397].

Schultz teaches a binding substrate, but fails to teach that the binding substrate has a molecular imprint of the analyte.

Vo-Dinh, however, teaches the use of a molecular imprint material designed to concentrate specific compounds of interest for improved sensitivity (column 6, lines 63-65).

Therefore it would have been obvious to use a molecular imprint material, as suggested by Vo-Dinh, in the device of Schultz, in order to concentrate specific compounds of interest for improved sensitivity.

15. Claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435], as applied to claim 1 above, and further in view of Nardone et al [US 6,531,581].

Schultz teaches a dye that quenches the signal produced by a fluorescent label when the analyte analog is covalently attached to the receptor material, as discussed above. Schultz does not teach that the quenching dye is Alkali blue.

Nardone et al, however, do teach the use of Alkali blue as a quenching dye (column 5, line 1), since fluorescent dyes may have fluorescent emissions that will spill into assay wavelengths and increase the background noise (column 5, lines 63-67).

Therefore it would have been obvious to use non-fluorescent dyes such as Alkali blue as quenching dyes instead of a rhodamine dye molecule in the device of Schultz, as suggested by Nardone et al, in order to prevent fluorescent emissions that would spill into assay wavelengths, thus increasing the background noise.

16. Claims 27, 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435], as applied to claim 1 above, and further in view of Ferri et al [Ferri et al, Direct eye visualization of Cfluorescence for immunocytochemistry and in situ hybridization, 2000, J Hist Cytochem, 48(3), 437-444]

Schultz and Krauth teach the use of a reference, as discussed above, but do not teach the use of cyanine dyes such as Cy5.

Ferri et al, however, teach that Cy5 provides a distinct fluorescent signal that can easily be separated from that of many other fluorochromes (p.437, col.1). Ferri et al

further teach that a distinct advantage of Cy5 is the low autofluorescence found in many cells and tissues in the above wavelength range (p.437, col.1).

Therefore, it would have been obvious to use Cy5 as a reference in the device of Schultz and Krauth, as suggested by Ferri et al, in order to provide a distinct fluorescent signal that can be easily separated from other fluorochromes.

17. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435], as applied to claim 1 above, and further in view of Panchuk-Voloshina et al [Panchuk-Voloshina et al, Alexa Dyes, a series of new fluorescent dyes that yield exceptionally bright, photostable conjugates, 1999, J Hist Cytochem, 47(9), 1179-1188].

Schultz and Krauth teach the use of a reference as discussed above, but do not teach the use of ALEXA FLUOR dyes such as ALEXA 488.

Panchuk-Voloshina et al, however, teach that ALEXA dyes yield the most stable conjugates and allows reactions to take place efficiently at pH 7.5-8.5 or at even lower pH when required (p.1180, col.1).

Therefore it would have been obvious in the method of Schultz to substitute the fluorescein label with ALEXA 488, as taught by Kumar et al, since it has been demonstrated to be more immunofluorescence than fluorescein for conventional immunofluorescence.

18. Claims 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435], as applied to claim 1 above, and further in view of Bruchez et al [US 6,274,323].

Schultz and Krauth teach the use of a reference, as discussed above, but fail to teach the use of quantum dots as a reference.

Bruchez et al, however, teach that semiconductor nanocrystals may be used to detect or track a single target, and can be used to in a variety of assays where other, less reliable, labeling methods have typically been used, including fluorescence microscopy, histology, cytology pathology, flow cytometry, FISH, signal amplification assays, DNA and protein sequencing, immunoassays, immunohistochemical analysis, homogeneous assays, high throughput screening, and the like (column 16, lines 58-67).

Therefore it would have been obvious to use semiconductor nanocrystals, or quantum dots, instead of a label as a reference in the device of Schultz, as suggested by Bruchez et al, in order to provide a more reliable labeling method.

Double Patenting

IV. Claims 1-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of U.S. Patent No. 6,454,710. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent teaches labeled analogues which bind reversibly to a substrate, located within a support, a membrane, and a dye which absorbs a majority of the excitation and emission wavelengths of the fluorescent label (claim 1).

19. Claims 1-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-55 of U.S. Patent No. 6,379,622. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent teaches a labeled analogue, a reference comprising

quantum dots, a dye bound to a binding substrate with an absorption spectrum that has an absorption spectrum that overlaps the excitation and emission spectra of the label (claim 1).

Conclusion

VI. [redacted]

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BAO-THUY L. NGUYEN
PRIMARY EXAMINER

Nelson Yang
Patent Examiner
Art Unit 1641